Remarks

The amendment to the specification was made to incorporate the ATCC Deposit Designations for the recited hybridomas and antibody heavy and light chain sequences. The amendment was therefore made to address an informality. As such, the amendments do not add new matter and entry thereof is respectfully requested.

Respectfully submitted,

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Thus, in accordance with the invention, there are provided human CD40 antibodies that bind to CD40 (e.g., human CD40). In one embodiment, a CD40 antibody modulates one or more activities of CD40 (e.g., a signaling activity). In one aspect, a CD40 antibody of the invention decreases a CD40 activity (e.g., CD40L induced CD95 expression is reduced or blocked or cell proliferation is inhibited). In another aspect, a CD40 antibody of the invention increases a CD40 activity (e.g., CD40L induced CD95 expression is increased or stimulated or cell proliferation is increased or stimulated).

As used herein, the terms "CD40 antibody" or "anti-CD40 antibody" means an antibody that specifically binds to CD40. "Human CD40 antibody" or "human anti-CD40 antibody" mean that the antibody that specifically binds to CD40 consists of human immunoglobulin amino acid sequences. A human CD40 antibody that binds human CD40 is an antibody comprising human immunoglobulin amino acid sequences which specifically binds to human CD40, although the antibody may also bind to a non-human sequence that has an epitope that the human CD40 antibody recognizes.

CD40 antibodies of the invention include polyclonal or monoclonal antibodies, as well as fragments and modified forms as set forth herein. Pooled polyclonal and monoclonal antibodies containing two or more different CD40 antibodies with different binding specificity, binding affinity or functions are also provided.

CD40 antibodies of the invention contain kappa or lambda chain sequences. Each antibody molecule contains two kappa or two lambda light chains. The primary difference between kappa and lambda light chains is in the sequences of the constant region. In humans, the kappa chain variable region sequences have more diversity than lambda chain variable region sequences which results in the generation of more different (diverse) antibodies. Exemplary CD40 antibody produced by hybridoma F4-465 contains a human lambda light chain.

Exemplary antibodies are denoted as nos. 11 (ATCC PTA-2308), 30, 72 (ATCC PTA-2309) and 366 or are produced by the hybridomas denoted as F1-102 (ATCC PTA-3337), F2-103, F5-77, F5-152, F5-157, and F4-465 (ATCC PTA-3338). Although not wishing to be bound by theory, exemplary CD40 antibodies that inhibit a CD40 activity, e.g., nos. 30, 72, 366 and antibody produced by hybridoma F4-465 appear to decrease binding of CD40L to CD40 and do not induce

therapeutic agents or virus vectors for gene therapy. Another example is thrombus formation, artherosclerosis or vessel intimal thickening in a subject.

Examples where increasing a CD40 activity can result in a physiological effect include stimulating an immune response to an infectious agent (e.g., a poorly immunogenic pathogen) or a cancer, or increasing the ability to respond to an antigen by improving memory of cell mediated immunity or humoral immunity. Stimulating cell survival or proliferation of immune cells by stimulating CD40 can also result in treatment.

Invention CD40 antibodies include antibodies having the binding specificity of the CD40 antibodies exemplified herein. Thus, in another embodiment, the invention provides CD40 antibodies having the binding specificity of the antibodies denoted as nos. 11, 30, 72 and 366, and the antibodies produced by the hybridomas denoted as F1-102, F5-152, F2-103, F5-77, F5-157 and F4-465. In one aspect, a CD40 antibody has a heavy or light chain sequence as set forth in SEQ ID NOs:10 (ATCC PTA-3302), 11 (ATCC PTA-3303), 12 (ATCC PTA-3306), 13 (ATCC PTA-3307), 14 (ATCC PTA-3304) or 15 (ATCC PTA-3305).

As used herein, the term "binding specificity," when used in reference to an antibody means that the antibody recognizes the same antigenic epitope as a comparison antibody. Thus, a CD40 antibody having the binding specificity of the antibody denoted as no. 11 recognizes the same epitope as the CD40 antibody denoted as no. 11; a CD40 antibody having the binding specificity of the antibody denoted as no. 72 recognizes the same epitope as the CD40 antibody denoted as no. 72; a CD40 antibody having the binding specificity of the antibody produced by the hybridoma denoted as F1-102 recognizes the same epitope as the antibody produced by the hybridoma denoted as F1-102; and so on and so forth.

Typically epitopes are short amino acid sequences, e.g. about five amino acids in length. Systematic techniques for identifying epitopes are known in the art and are described, for example, in U.S. Patent No. 4,708,871. Briefly, a set of overlapping oligopeptides derived from the CD40 antigen may be synthesized and bound to a solid phase array of pins, with a unique oligopeptide on each pin. The array of pins may comprise a 96-well microtiter plate, permitting one to assay all 96 oligopeptides simultaneously, e.g., for binding to an anti-CD40 monoclonal antibody. Alternatively, phage display peptide library kits (New England BioLabs) are currently commercially